(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 November 2002 (14.11.2002)

PCT

(10) International Publication Number
WO 02/089725 A2

(51) International Patent Classification[7]: A61J

(21) International Application Number: PCT/US02/14849

(22) International Filing Date: 7 May 2002 (07.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/289,429 8 May 2001 (08.05.2001) US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 02/089725 A2

(54) Title: FLUID TRANSFER DEVICES AND METHODS OF USE CROSS REFERENCE TO RELATED APPLICATIONS

(57) Abstract: A device and method of use are disclosed to facilitate fluid transfers during sterile closed system processing procedures. The device is configured to create connections for the transfer of fluid between various components, along a closed sterile fluid passageway and, eventually, either to a fluid container or to a patient. As a result, the device and method of use of the present invention reduce the risk of contamination to the fluids, such as reagents, medicaments and cellular products, and increase user or technician safety during processing procedures.

FLUID TRANSFER DEVICES AND METHODS OF USE

CROSS REFERENCE TO RELATED APPLICATIONS

The present application claims priority to U.S. Provisional Patent Application No. 60/289,429, filed May 8, 2001, whose contents are fully incorporated herein by reference.

BACKGROUND OF THE INVENTION

The medical industry utilizes a wide variety of solution containers, container caps, connectors and tubing sets to create connections for the transfer of fluid between various components, along a fluid passageway and, eventually, either to a fluid container or to a patient. Examples of such connections include, but are not limited to, the processing of blood and its fractions, mixing of sterile solutions and connecting Foley catheters with urinary drainage bags. In order to maintain the sterility of the fluid pathway and minimize the risk to the operator (e.g., needle sticks, biohazard exposure, etc.), these connections should be designed to be closed (i.e., without open exposure of the fluid pathway to air).

In closed system cellular processing, for example, single use sterile disposable sets (e.g., bags, tubing, etc.) are joined together to enable the closed handling of biological fluids. One or more access points into sterile disposable sets are key to user convenience and system flexibility in closed system processing. All additions and removal of fluid (e.g., sampling, etc.) and connections of sets or other components for a next processing step are made via these access points. Access points are typically terminal tubing connectors such as luer fittings, spike couplers and bag ports (e.g., spikable membrane ports).

Luer connectors are widely used in the medical industry for making a connection between medical devices to establish a fluid passageway. In general, a luer connection assembly includes a male luer tip component or fitting having a frustoconical shape that is inserted into a female luer component or fitting having a frustoconically shaped receiving cavity. The opposing conical surfaces of the luer fittings come into contact and form a sealed friction fit assembly.

These connection assemblies and associated components are typically packaged in sterile packaging and include caps or protectors to maintain the sterility of the fluid pathway prior to use. However, at the time the actual connection between components is made, the fluid contacting surfaces and passageways are open to the

environment. As a result, these connections must frequently be made inside a laminar flow hood to mitigate the fluid contamination risk.

Another example of an access point or terminal connector is a spike coupler. A tubing set having a spike coupler as its terminal connector may be fluidly connected to a bag having a spikable membrane port. In general, a spike coupler assembly includes a spike component having a needle-like shape with a beveled tip that is inserted into a spikable membrane port generally having a cylindrically shaped receiving cavity or opening. The opposing surfaces of the spike coupler and membrane port come into contact and form a sealed friction fit assembly. The spike coupler is used to access the contents of the bag through the membrane port. When the spike is inserted into the port, the membrane is broken causing the fluid to flow from the container through the spike and into the tubing set. In contrast to the above-described luer connectors, sets joined via spike couplers and spikable membrane ports maintain an aseptic fluid pathway. This processing system has the advantages of reduced potential for contamination of the contained fluid and reduced potential for operator exposure to the biohazards presented by such fluids.

Common problems or drawbacks associated with more complicated processing using sets with spike couplers include exceeding the number of available access points on a particular disposable set or similar component. In these situations, it is often necessary to transfer the fluid to a new set in order to increase accessibility. Moreover, sets or containers having incompatible terminal connectors, such as both sets terminating in spike couplers, further adds to the difficulties encountered during more complicated processing and may render the closed system fluid transfer process an impossibility altogether.

In view of the foregoing, it would be desirable to have a unitary one-piece adapter or connector which enables the connection of two incompatible spike couplers. The adapter should also include an integral cover to maintain sterility when the adapter is not in use. As such, it is also desirable that the lumen and/or passageway through the adapter that forms a portion of the fluid passageway be sterile prior to use and maintain sterility, such as by being sealed against microbial ingress, during connection and disconnection of the spike couplers.

It is a further object of the present invention to provide a connector which is capable of being manufactured at high speeds and low cost. Generally the lower the number of parts making up a component, the lower the number of required molds and

high speed assembly devices, both of which generally translate to lower capital expenditures and therefore lower costs. It is a related object of the present invention to provide a connector which may be manufactured with a very low number of potential defects.

Depending on the application, many other features may also be desirable. Dead spaces or voids within the connector which cannot be "flushed" and in which stagnant fluid can collect to form a media for microbial growth should be minimized or eliminated. It is a related object of the present invention to provide a connector which forms a sealed fluid path such that a minimum number of microbes enter the fluid path during operation using aseptic techniques. Also, priming volume for the connector should be minimized.

It is still a further object of the present invention to provide a connector which minimizes or eliminates flow restrictions for the flow of fluid through the connector. It is another object of the present invention to provide a connector device which is capable of providing for a large number of connections and disconnects while maintaining the ability to seal against fluids under pressures typically found in an administration set.

For some processing procedures, it is necessary to transfer the fluid from a manufacturer provided open container, such as a bottle, to a differently configured closed container, such as a bag, to perform the closed system processing procedure. In this instance the user must pipette or decant the bottle contents into the secondary container inside of a laminar flow hood. This is an open and laborious process which, as a consequence, increases the potential for contamination of the fluid and exposure to the operator. In this instance, there is a need for a coupler that will facilitate the transfer in a closed and sterile fashion.

An analogous need also exists in open system centrifugation separation procedures. It is common in the medical, cell processing and other fields to separate cells from suspending fluids via centrifugation. This operation is typically required when washing cells. The fluid component of the separation is aspirated or decanted from the pellet of cells resulting from the applied centrifugal forces. While sample volumes of 500 ml or greater may be washed in bags using closed automated systems currently available on the market, smaller volumes are typically washed using commercially available open conical tubes. This is due to the cell loss associated with bag use. In particular, cells become trapped along the seams of bags and the flexible

materials/structure of bags cause their contents to move during handling, thereby dislodging the cells from their concentrated pellet formation. Therefore, a connector or system that enables the integration of rigid open vessels with closed flexible containers is needed.

Although rigid containers overcome these shortcomings typically associated with flexible bags, the use of rigid containers requires access to air. This is due to the fact that it is not possible to add or subtract fluids from such a container and maintain a constant volume inside the rigid closed container. Typically, a volume of air is needed to compensate for removed/added fluids. For example, the removal of 200 ml of fluid results in the addition of an equal amount of air into the container and, thereby, into contact with the fluid path. As a result, the addition of air into the container potentially increases the risk of fluid and system contamination. Therefore, a connector or system that enables the addition and/or release of air/gases into a container without increasing the risk of fluid and system contamination and operator exposure is needed.

BRIEF SUMMARY OF THE INVENTION

In view of the foregoing, it is an object of the present invention to provide a connector or cap-shaped device that is capable of being manufactured at high speeds and low cost.

It is a further object of the present invention to provide a connector or cap-shaped device which may be manufactured with a very low number of potential defects.

It is a further object of the present invention to provide a connector or cap-shaped device which forms a sealed fluid path such that a minimum number of microbes enter the fluid path during operation using aseptic techniques.

It is a further object of the present invention to provide a connector or cap-shaped device which minimizes or eliminates flow restrictions for the flow of fluid through the connector.

It is a further object of the present invention to provide a connector or cap-shaped device which is capable of providing for a large number of connections and disconnects while maintaining the ability to seal against fluids under pressures typically found in an administration set.

It is a further object of the present invention to provide a coupler or cap-shaped device that will facilitate the transfer of fluids in a closed sterile fashion.

It is a further object of the present invention to provide a connector or system that enables the integration of rigid open vessels with closed flexible containers.

It is a further object of the present invention to provide a connector or system that enables the addition and/or release of air/gases into a container without increasing the risk of fluid and system contamination and operator exposure.

These and other objects not specifically enumerated her are addressed by the present invention which in at least one embodiment may include a fluid transfer device that includes a cap-shaped device including a first port and a second port. The device may further include a filtration vent extending from the first port, wherein the filtration vent filters air passing through the filtration vent, and a tubing segment assembly extending from the second port and forming a passageway for fluid transfers. In general, the passageway formed by the device is a closed fluid pathway. In addition, the device may be configured for attachment to a container, such as a rigid container, bottle, conical tube, centrifugation tube, centrifugation container, etc., or prefabricated onto a container and provided as an integral device.

The present invention may further include a method of transferring fluids into and out of a container comprising removing a cap form a container while under a laminar flow hood and installing a cap-shaped device onto the container. The method may also include transferring the container to a general laboratory environment and connecting a closed system set to a tubing segment assembly of the cap-shaped device, whereby a fluid may be transferred into or out of said container in a closed system fluid pathway. The method may further include transferring a fluid from the closed system set into the container, centrifuging the fluid and removing a portion of the fluid from the container.

In an alternate embodiment, the method may include pumping a fluid from a container through a second tubing segment of the cap-shaped device, through a tubing segment assembly and into a closed system set.

A further embodiment of the present invention may include a method of transferring fluids into or out of a container comprising addling a fluid to a container via a cap-shaped device of the container in a general laboratory environment, wherein a fluid pathway of the container and cap-shaped device is a closed system fluid pathway. The method may also include centrifuging the fluid within the container and removing a portion of the fluid from the container while maintaining the closed system fluid pathway. The method may further include connecting a receiving container to the

closed system set, positioning the receiving container a sufficient distance below the container and aspirating fluid from the container to the receiving container.

BRIEF DESCRIPTION OF THE DRAWINGS

Other features and advantages of the present invention will be seen as the following description of particular embodiments progresses in conjunction with the drawings, in which:

Figure 1 is a perspective view of a dual port membrane adapter device in accordance with an embodiment of the present invention;

Figure 2 is illustrates the assembly and internal components of the adapter device in accordance with an embodiment of the present invention;

Figure 3 is an end view of the adapter device in accordance with an embodiment of the present invention;

Figure 4 is an end view of an alternate embodiment of the device of the present invention;

Figure 5 is a sectional view of the adapter device in accordance with an embodiment of the present invention;

Figure 6 illustrates a cap-shaped device in accordance with an embodiment of the present invention;

Figure 7 is a perspective view of the cap-shaped device in accordance with an embodiment of the present invention;

Figure 8 is an alternate view of the cap-shaped device in accordance with an embodiment of the present invention;

Figure 9 illustrates an alternate embodiment of the cap-shaped device in accordance with the present invention;

Figure 10 illustrates a method of using the adapter in accordance with an embodiment of the present invention; and

Figure 11 illustrates a method of using the cap-shaped device in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The following description and figures are meant to be illustrative only and not limiting. Other embodiments of this invention will be apparent to those of ordinary skill in the art in view of this description.

Referring to Figure 1, an embodiment of a fluid transfer device in accordance with the present invention includes a connector or adapter 10 having a first

cylindrically shaped conduit 12, a second cylindrically shaped conduit 14, and a hollow, cylindrically shaped sleeve 16 located between the first and second conduits 12,14 of the adapter 10. Each conduit 12,14 and the sleeve 16 include a first end, a second end and a passageway extending therebetween for the passage of fluid. The conduits 12,14 and sleeve 16 are aligned along the same longitudinal axis 13 and are configured in fluid flow relationship with each other.

In one embodiment of the device, the first end 18 of the first conduit 12 includes a fluid inlet port 20 and the second end 22 of the second conduit 14 includes a fluid outlet port 24. Alternatively, the first end 18 of the first conduit 12 may include a fluid outlet port 20 and the second end 22 of the second conduit 14 may include a fluid inlet port 24. In general, the conduits 12,14 are configured for quick connection for releasably engaging a terminal end, such as a spike coupler, of a tubing set.

As shown in Figures 1, 2 and 3, each conduit 12,14 is approximately 1.00 $\pm$ 0.05 inch (25.40 $\pm$ 1.27 mm) in length LC. The tubular wall 26 forming the structure or framework of each conduit 12,14 may include a smooth internal surface 28, a smooth external surface 30 and a wall thickness TC. In one embodiment of the adapter 10, the wall thickness TC, internal diameter IDC and external diameter EDC of each conduit are approximately within the range of 0.030 $\pm$ 0.005 inch (0.762 $\pm$ 0.127 mm), 0.190 $\pm$ 0.005 inch (4.826 $\pm$ 0.127 mm) and 0.250 $\pm$ 0.005 inch (6.350 $\pm$ 0.127 mm), respectively. The diameters and wall thickness may either be uniform or variable along the longitudinal length of each conduit 12,14. A particular choice of wall thickness, diameters and length depends on the configuration of the mating terminal end intended for connection to the adapter 10. In other words, the configuration of each conduit 12,14 can vary according to the intended procedure, mating connection and usage.

Similarly, the dimensional configuration of the sleeve 16 of the adapter 10 should be appropriately sized to surround and overlap portions of the conduits 12,14 and to provide a sufficient flow path for connecting devices (e.g., tubing set spike couplers). In one embodiment, the length LS of the device sleeve 16 may be approximately within the range of 1.50 $\pm$ 0.05 inch (38.10 $\pm$ 1.27 mm). In addition, the overlap portions 32 of the conduits 12,14 and sleeve 16 may each be within the range of 0.25 $\pm$ 0.05 inch (6.35 $\pm$ 1.27 mm).

The tubular wall 34 forming the structure of the sleeve 16 may include a smooth internal surface 36, a smooth external surface 38 and a wall thickness TS. In one

embodiment, the wall thickness TS, internal diameter IDS and external diameter EDS of the sleeve 16 are approximately within the range of 0.030 ± 0.005 inch (0.762 ± 0.127 mm), 0.245 ± 0.005 inch (6.223 ± 0.127 mm) and 0.305 ± 0.005 inch (7.747 ± 0.127 mm), respectively. As with the conduits 12,14, the diameters and wall thickness of the sleeve 16 may either be uniform or variable along the length of the sleeve. In general, the internal diameter IDS of at least a portion of the sleeve 16 should be appropriately sized to match at least a portion of the external diameter EDC of each conduit 12,14 to ensure that there is a snug and conforming fit and contact between the opposing external and internal surfaces 30,36 of each conduit 12,14 and sleeve 16, respectively. Further, the internal diameters of both the conduits 12,14 and sleeve 16 should be large enough to adequately support an unrestricted flow of fluid therethrough. Overall, the design of the adapter 10 should facilitate the connection of tubing lines that terminate in spike couplers.

In an alternate embodiment of the invention (not shown), the opposing external and internal surfaces 30,36 of each conduit 12,14 and sleeve 16, respectively, may be textured to increase the surface area and, thereby, further enhance the contact characteristics of the surfaces of the friction fit assembly 10. In yet another embodiment of the device 10, the opposing external and internal surfaces 30,36 of each conduit 12,14 and sleeve 16, respectively, may be threaded for threaded engagement between the components of the adapter 10. Alternative engagement features and configurations including, but not limited to, ridges, channels, grooves, bumps, indents, prongs, rods, tabs, flanges, chamfers, and threads are also included within the scope of the claimed invention.

The conduits 12,14 and sleeve 16 of the adapter 10 may be further secured together via ultrasonic welding. Additional techniques and methods used to secure together the components of the assembly 10 include, but are not limited to, frictional welding, chemical bonding, heat shrinking, and fusing. These and other techniques and methods not specifically disclosed herein but known to those skilled in the art are also included within the scope of the claimed invention.

In addition to the particular dimensional attributes of the conduits 12,14 and sleeve 16, the material characteristics of the adapter 10 are also important to achieve the desired performance features of the device 10. A variety of materials may be used to fabricate the adapter 10 of the present invention. These materials include, but are not limited to, plastics (e.g., polyethylene, polyvinyl chloride, polycarbonate, etc.),

silicone, stainless steel, metals, and ceramics, including combinations thereof. In general, the adapter materials should be sterilizable, biocompatible and non-pyrogenic.

Although the adapter 10 may be constructed as a rigid, flexible or semi-flexible connector, it is preferred that the materials together with the structural design of the adapter 10 provide sufficient strength and structural integrity to avoid kinking, collapse or restriction of the closed fluid flow path of the conduits 12,14 and sleeve 16. In one embodiment of the invention, the adapter 10 may be configured as single use, disposable connector. Alternatively, the adapter 10 may be configured as a multiple use and re-sterilizable device.

Referring to Figures 2 and 3, each conduit 12,14 of the adapter 10 includes a transverse diaphragm or membrane 40 adapted for breakage by a spike coupler from a tubing set. The membrane 40 may be located anywhere along the longitudinal length of the conduits 12,14 and, preferably, is located near the mid-section of each conduit 12,14. In one embodiment of the invention, the membrane 40 is located approximately within the range of $\pm$ 0.125 inch ($\pm$ 3.1750 mm) from an end 42 of the sleeve 16 when the conduit 12,14 is housed within the sleeve 16. As a result, the two membranes 40 of the adapter 10 form a closed chamber that extends along the length LS of the sleeve 16 and a portion 42 of the length LC of each conduit 12,14.

In one embodiment of the invention, the membrane 40 is formed as a solid, resilient barrier capable of being pierced or broken when a terminal connector (e.g., spike coupler) is properly seated within the adapter 10. In an alternate embodiment, shown in Figure 4, the membrane 40 may include one or more slits 44 forming a valve-like element capable of being re-sealed in its closed configuration. For example, when a spike coupler penetrates the membrane 40, the slit(s) 44 spread apart and form an opening in the membrane 40 that substantially surrounds a portion of the spike coupler. The resulting connection between the spike coupler of the tubing set and the conduit 12,14 of the adapter 10 forms a closed fluid pathway, thereby minimizing, if not altogether eliminating, contamination risks. When the spike coupler is removed or disconnected from the adapter 10, the slit(s) 44 return to their original closed configuration and, essentially, re-seal the opening in the membrane 40. As such, the adapter 10, particularly the chamber of the adapter 10, maintains a continuous, closed, contamination-free system that seals the fluid passageway from the environment before, during and after a connection is formed.

Each membrane 40 of the present invention may be fabricated from essentially the same materials of the conduits 12,14 and sleeve 16, as previously described. In an alternate embodiment, the membranes 40, conduits 12,14 and/or sleeve 16 of the device 10 may be fabricated from dissimilar materials. In a preferred embodiment, the membrane material is resilient and includes memory-characteristics that enable the membrane to return to its original configuration after use and adequately seal the fluid path of the system.

As shown in Figure 5, the adapter 10 of the present invention may include one or more covers or tip protectors 46 to shield the fluid inlet port and fluid outlet port of the conduits 12,14 from damage and contamination risks. These protectors maintain the sterility of the membrane portion of the connector during storage and up to the time of use.

As noted in the Background of the Invention as set forth above, in addition to connectors, other types of fluid transfer devices used in the medical industry include container caps and closed container devices. Referring to Figure 6, a cap-shaped device in accordance with the present invention may include a sterile filtration vent 52 and a tubing segment assembly 54. In general, the cap-shaped device 50 includes a cylindrical neck 56 and a substantially planar surface 58 positioned perpendicular to the longitudinal axis 53 of the neck 56 and device 50.

To accommodate a variety of processing procedures and container configurations, the cap-shaped device 50 may be configured as a rigid or semi-flexible component. In one embodiment, the cylindrical neck 56 of the device 50 is configured for attachment to a bottle, conical tube, or other fixed volume fluid container. However, it should be noted that alternate configurations of the neck 56 including, but not limited to, square-shaped, oval, and polygonal are known in the art and, as such, are also included within the scope of the claimed invention.

Two or more access ports or openings 60 are provided on the surface 58 of the device 50, as shown in Figure 7. In one embodiment of the invention, a sterile filtration vent 52 may extend from the first access port 60 and a tubing segment assembly 54 may extend from the second access port 60. Referring to Figure 6, the sterile filtration vent 52 may include a sterile, tubular or luer-shaped element 62 having a filter (not shown) located within the interior cavity of the element 62. Before ambient air may enter or leave the system, it must first pass through the filer of the vent 52. As such, the sterile filtration vent 52 accomplishes several goals of the present invention.

First, by filtering ambient air before it enters the system, the sterile filtration vent 52 maintains system sterility and reduces the probability of fluid and system contamination. In addition, since entrapped gases/air must also pass through the filter before leaving the system, user exposure to such potentially toxic and harmful gases/air is significantly reduced or completely eliminated by virtue of the vent 52. Further, with respect to fluid transfer operations using rigid containers, the sterile filtration vent 52 allows air and gases to enter/escape through the vent 52 and into/out of the closed rigid container to compensate for removed/added fluids, while maintaining sterility of the system via the filter.

Referring to Figures 6 and 8, the tubing segment assembly 54 of the device 50 of the present invention may include a segment of tubing 64 and a sterile tubular or luer-shaped element 66. A first end 68 of the luer-shaped element 66 may extend from the second access port 60 of the device 50 and a second end 70 of the luer-shaped element 66 may be in communication with a first end 72 of the tubing segment 64. Extending from the second end (not shown) of the tubing segment 64 may be a terminal end of another closed system sterile disposable set used to access to the contents of the container.

In one embodiment of the invention, a second tubing segment 74 may also extend from the second access port 60 and/or first end 68 of the luer-shaped element 66 within the interior portion 76 of the cap-shaped device 50, as shown in Figure 8. This second tubing segment 74 may be used as a straw or wick to access the contents of the container during use of the device 50, as further described below. Depending on the particular function or procedure, the length of the second tubing segment may vary. For example, in a large volume bottle cap, the tube 74 may extend to the bottom of the bottle and be configured with a beveled or other similar non-blunt end. This design would facilitate removal of the contents by pumping when the container is in an upright position.

Analogously, when the cap-shaped device 50 is fitted onto a centrifuge tube with a conical bottom, the second tubing segment 74 may extend to varying levels or depths towards the conical bottom. In essence, the level or lengths of the second tubing segment 74 dictates the lowest level of fluid which may be aspirated from a container.

In an alternate embodiment, the second tubing segment 74 may extend through the second access port 60 of the device 50 (not shown). For this embodiment, the

second tubing segment 74 may be mated to the cap 50 in such a way as to enable a hermetic seal while allowing for user manipulation of tubing depth within the container to thereby access a variety of fluid levels.

As with the adapter 10, the connector or cap-shaped device 50 of the present invention may be fabricated from a variety of materials, such as those previously described herein. In general, the device materials should be sterilizable, biocompatible and non-pyrogenic. Together with the materials, the particular dimensional characteristics of the device 50 should be optimized to achieve the desired performance features of the device 50, such as desired fluid flow rates and sufficient venting. In particular, the vent 52 may be configured to include an adequate flow-through and filtration area to enable free fluid flow from the tube 54. In addition, the tubing segments 64,74 may be configured as flexible, semi-flexible or rigid components, depending upon the desired performance characteristics of the device 50. Generally, in the field of closed system cellular processing, the device 50 should be configured to allow fluid transfers and processing to be conducted in the open laboratory environment, without the risk of contaminating the reagents and cellular products and exposing technicians to contamination during the procedure.

In one embodiment of the invention, the cap-shaped device 50 may be supplied to users in several conventional container (e.g., bottle, bag, tube, etc.) bottle sizes to accommodate a variety of bottled reagents. In another embodiment, the cap 50 may be pre-fabricated onto a container and provided as an integral device. In this regard, Figure 9 depicts an example of what this embodiment of a capped-container device 78 may look like in accordance with the present invention. In essence, the device 78 includes the cap-shaped device 50 and a container 79.

Although the container 79 depicted in Figure 9 is a conical tube, any of a variety of containers including, but not limited to, bottles and bags may be used and are also included within the scope of the claimed invention. In one embodiment, this container 79 may be supplied in an unfilled or empty state to enable user addition/subtraction of fluid. In addition, the cap-shaped device 50 may be either permanently or removably attached to the container 79. In an alternate embodiment, the container 79 may be supplied pre-filled with a solution, reagent or other desired fluid to bypass the need for cap placement entirely. Similar to the previous embodiment, the pre-filled cap-shaped device 50 may be either permanently or removably attached to the container 79.

Method of Use

In one embodiment of the invention, the double membrane port adapter 10 may be used in closed system cellular processing. As shown in Figure 10, one step of a typical cellular processing procedure may require two single use sterile disposable sets (e.g., tubing sets terminating in spike couplers) to be joined together for a fluid transfer operation. To join the sets, a spike coupler 80 of a first tubing set is inserted along the longitudinal axis of the adapter 10, through a port 20 and into a first conduit 12 of the device 10. The spike coupler 80 is then advanced further within the conduit 12 until at least the tip 82 of the spike coupler penetrates through the membrane 40 of the conduit 12 and the spike coupler 80 is properly seated within the adapter 10. At this point in the procedure, the fluid pathway of the first tubing set remains in a closed, sealed configuration due to the unbroken membrane 40 of the second conduit 14 of the adapter 10.

Next, a spike coupler 84 of a second tubing set is inserted along the longitudinal axis of the adapter, through a port 24 and into a second conduit 14 of the device 10. The spike coupler 84 is then advanced further within the conduit 14 until at least the tip 86 of the spike coupler 84 penetrates through the membrane 40 of the conduit 14 and the spike coupler 84 is properly seated within the adapter 10 (not shown). Penetration of the second spike coupler 84 through the membrane 40 of the second conduit 14 creates a closed, continuous, aseptic fluid pathway and, thereby, enables fluid to be transferred via the sets.

Closed system cellular processing methods may also require the transfer of fluid into or out of containers. In this instance, a cap-shaped device 50 may be used to provide added convenience for the user and processing flexibility. During use, a user of the device 50 would replace the manufacturer provided cap on a container with the cap-shaped device 50 of the present invention while under a laminar flow hood. As shown in Figure 11, the capped container 88 could then be removed to the general laboratory environment, where all fluid transfers of the processing procedure may be performed while using the device 50. Next, the tubing segment 64 on the cap-shaped device 50 could be connected to other closed system sterile disposable sets 90. As a result, fluid could then be transferred from the bottle 88 to the closed system sterile disposable set 90 through the tubing segment 64 via gravity by inversion of the bottle 88. In addition, if a rigid container is used, a volume of ambient air will enter the container/bottle 88 via the sterile filtration vent 52 to replace the lost volume of fluid

during the fluid transfer operation. As such, the tubing segment assembly 54 forms a closed system fluid pathway, together with the filtration vent 52, for maintaining the sterility of the system.

In an alternate embodiment, the fluid may be pumped out of the bottle 88, through the tubing segment 64 and into the disposable set 90. In yet another embodiment of the invention, the cap-shaped device 50 may be configured with a second tubing segment 74 inside the bottle. As a result, the bottle 88 could remain in an upright position and the fluid could be pumped out of the bottle 88 via the second tubing segment 74, through the tubing segment 64 and into the disposable set 90.

As a further convenience for the user and means to maintain system sterility, the processing procedure may be carried out using the cap-shaped device 50 configured onto a conical shaped tube/container 79, as shown in Figure 9. During the processing procedure, a cell suspension may be added to the container 79 by connecting the tubing segment 64 to another closed sterile set. The device 78 would be sealed (reversibly or irreversibly) and the whole apparatus 78 placed into a centrifuge. Next, the apparatus 78 would be centrifuged resulting in pelletization of the heavier cells or other particles from the fluid. After centrifugation, the apparatus 78 would be removed from the centrifuge and another connection would be made to the tubing segment 64, typically via an alternate distal connector. The fluid portion of the suspension may then be aspirated via the second tubing segment 74 into a closed receiving container (not shown) via gravity and capillary action. This process of aspirating the fluid from the container 79 may be accomplished by placing the receiving container a sufficient distance below the conical shaped tube 79 to draw off the fluid. Residual fluid in the bottom of the container 79 may be aspirated by slightly tipping the container 79 and without disturbing the cell pellet.

As previously described, the length of the second tubing segment 74 may be configured as desired to remain near the level of a cell pellet, yet not allow cells to become lodged there during centrifugation. It is clear that the tubing length might be longer to accommodate tubes of greater length. In additional embodiments of the invention, caps 50 (or full assemblies 78) may be made with different tubing lengths. As such, the user would simply decide which embodiment to use based on the chosen application.

In view of the foregoing, the cap-shaped device 50,78 of the present invention facilitates the addition of the bottled reagent or fluid to closed sets and, thereby,

reduces overall costs of processing procedures. In addition, the device 50,78 enables processing in an open laboratory environment by providing a closed system fluid path that reduces the risk of contamination to the reagents and cellular products and increases user or technician safety during processing procedures. In particular, the device 50,78 reduces the potential of exposure of the operator to potentially biohazardous materials.

Although the invention has been described in terms of particular embodiments and applications, one of ordinary skill in the art, in light of this teaching, can generate additional embodiments and modifications without departing from the spirit of or exceeding the scope of the claimed invention. Accordingly, it is to be understood that the drawings and descriptions herein are proffered by way of example to facilitate comprehension of the invention and should not be construed to limit the scope thereof.

What is claimed is:

1. A fluid transfer device comprising:

a cap-shaped device including a first port and a second port;

a filtration vent extending from said first port, wherein said filtration vent filters air passing through said filtration vent; and

a tubing segment assembly extending from said second port and forming a passageway for fluid transfers.

2. The device of claim 1 wherein said passageway is a closed fluid pathway.

3. The device of claim 1 wherein said cap-shaped device is configured for attachment to a rigid container.

4. The device of claim 3 wherein said container is a centrifugation container.

5. The device of claim 1 wherein said cap-shaped device is configured for attachment to a conical tube.

6. The device of claim 5 wherein said attachment is permanent.

7. The device of claim 5 wherein said attachment is removable.

8. The device of claim 5 wherein said conical tube is a centrifugation tube.

9. The device of claim 1 further comprising a second tubing segment extending from said second port within an interior portion of said cap-shaped device.

10. The device of claim 1 wherein said cap-shaped device is prefabricated onto a container and provided as an integral device.

11. A method of transferring fluids into or out of a container comprising:

removing a cap from a container while under a laminar flow hood;

installing a cap-shaped device onto said container;

transferring said container to a general laboratory environment; and

connecting a closed system set to a tubing segment assembly of said cap-shaped device, whereby a fluid may be transferred into or out of said container in a closed system fluid pathway.

12. The method of claim 11 further comprising:

inverting said container, whereby fluid flows in a closed system fluid pathway from said container to said closed system set via gravity.

13. The method of claim 11 further comprising:

transferring a fluid from said closed system set into said container.

14. The method of claim 13 further comprising:

centrifuging said fluid within said container; and

removing a portion of said fluid from said container.

15. The method of claim 14 further comprising:

connecting a closed system set to a tubing segment assembly of said cap-shaped device, whereby a fluid may be transferred into or out of said container in a closed system fluid pathway.

16. The method of claim 11 further comprising:

pumping a fluid from said container through a second tubing segment of said cap-shaped device, through said tubing segment assembly and into said closed system set.

17. A method of transferring fluids into or out of a container comprising:

adding a fluid to a container via a cap-shaped device of said container in a general laboratory environment, wherein a fluid pathway of said container and cap-shaped device is a closed system fluid pathway ;

centrifuging said fluid within said container; and

removing a portion of said fluid from said container while maintaining said closed system fluid pathway.

18. The method of claim 17 further comprising:

connecting a closed system set to a tubing segment assembly of said cap-shaped device, whereby a fluid may be transferred into or out of said container in a closed system fluid pathway.

19. The method of claim 18 further comprising:

connecting a receiving container to said closed system set;

positioning said receiving container a sufficient distance below said container; and

aspirating said fluid from said container to said receiving container.

20. The method of claim 19 further comprising:

tipping said container to remove any residual fluid from said container.

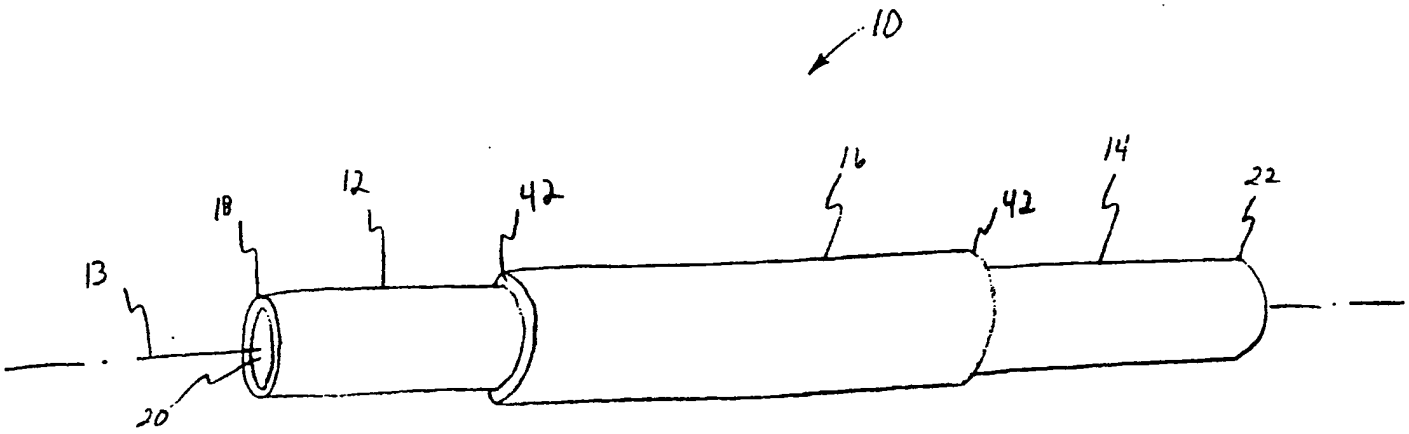

FIGURE 1

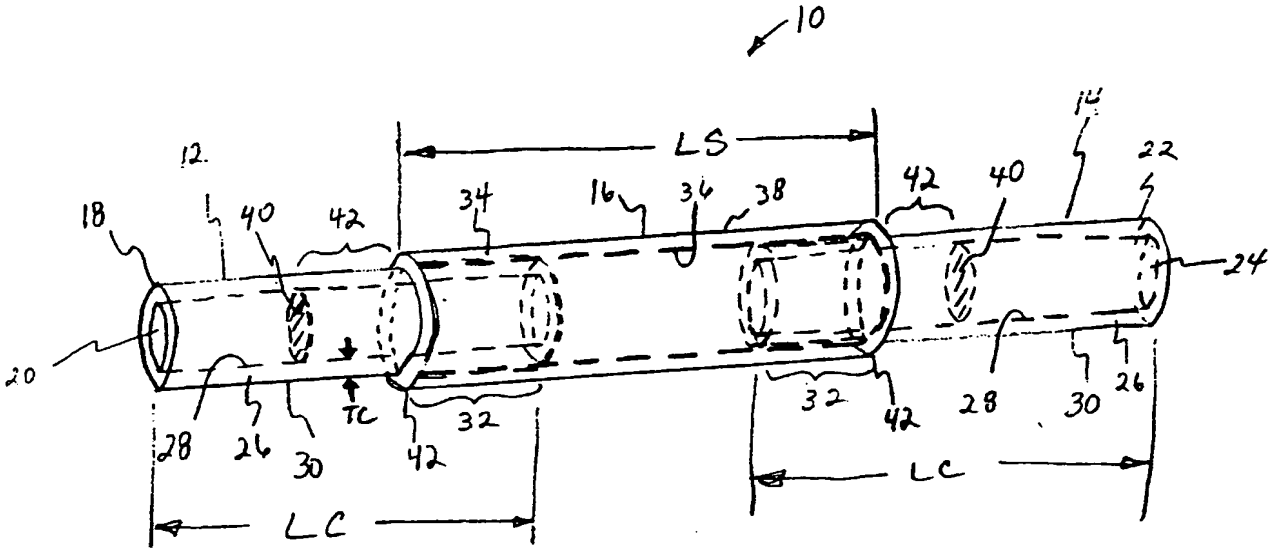

FIGURE 2

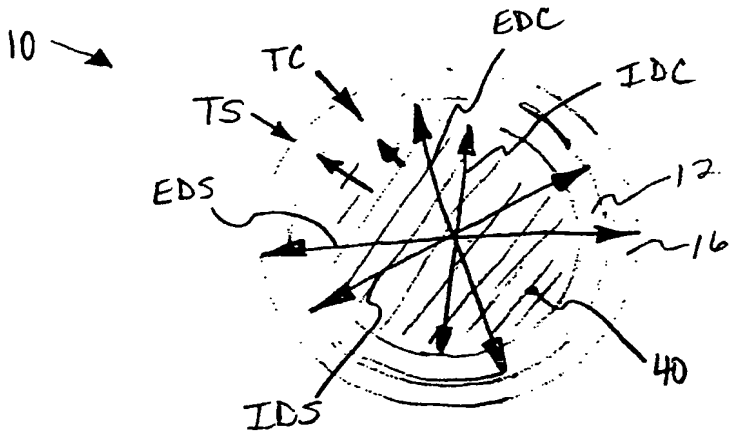

FIGURE 3

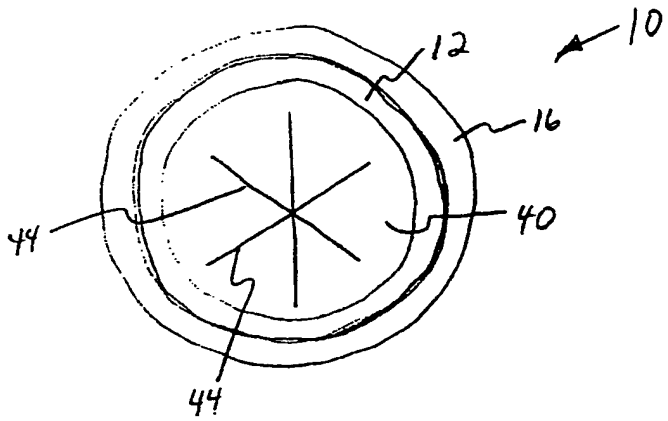

FIGURE 4

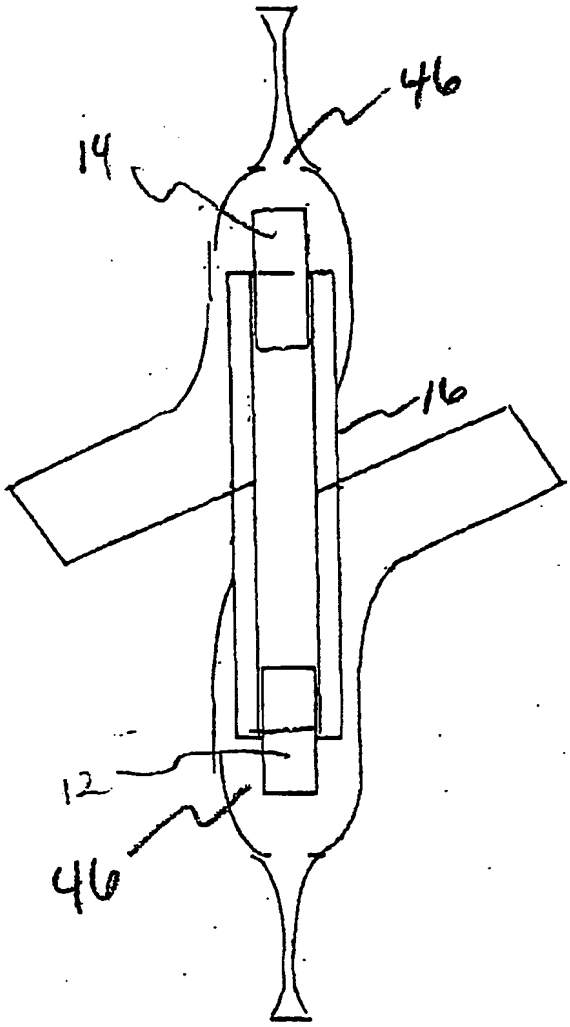

FIGURE 5

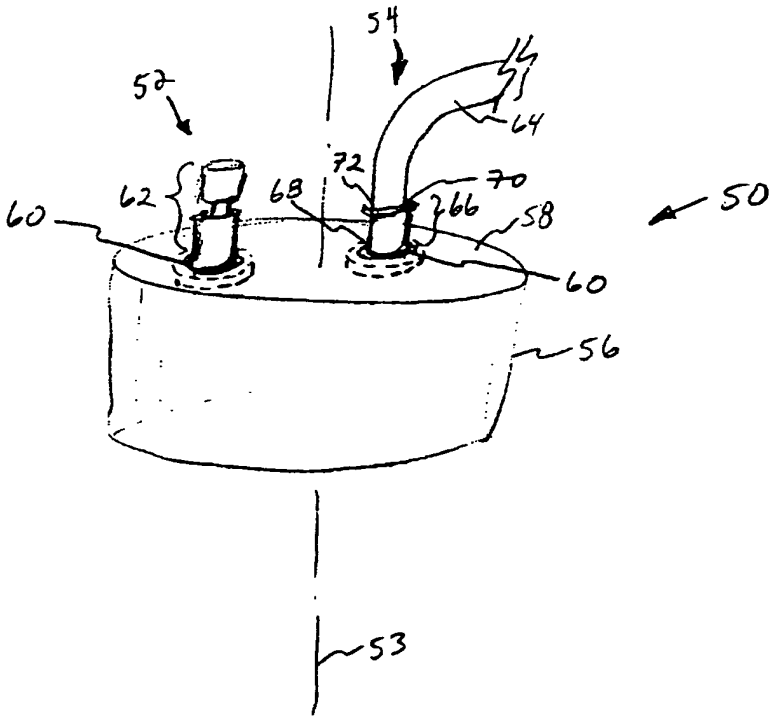

FIGURE 6

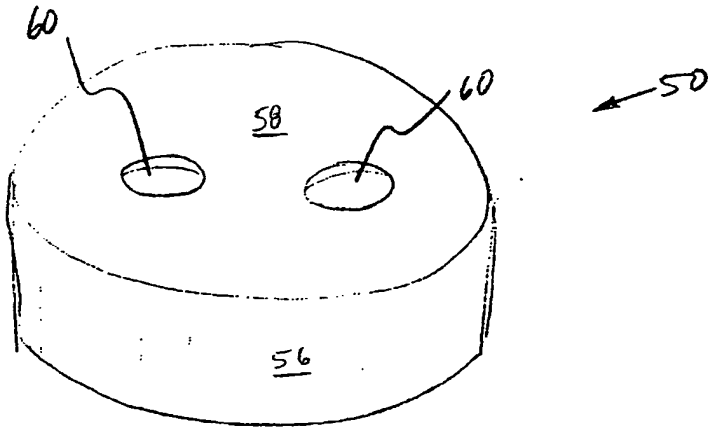

FIGURE 7

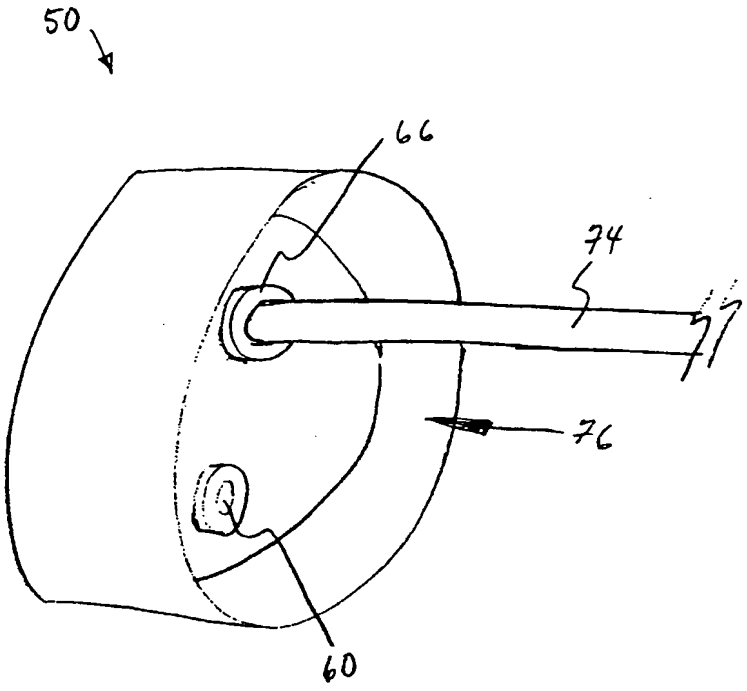

FIGURE 8

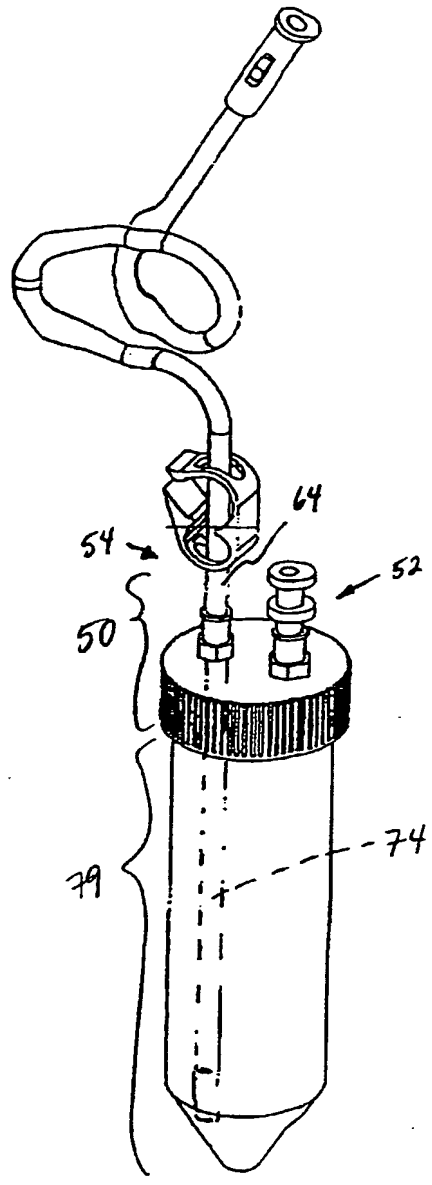

FIGURE 9

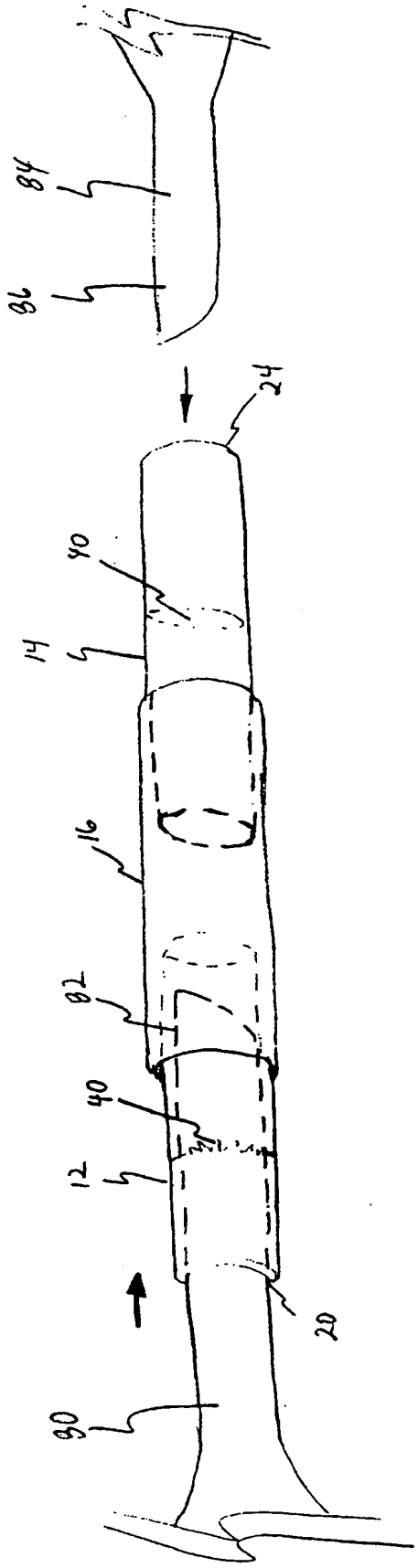

FIGURE 10

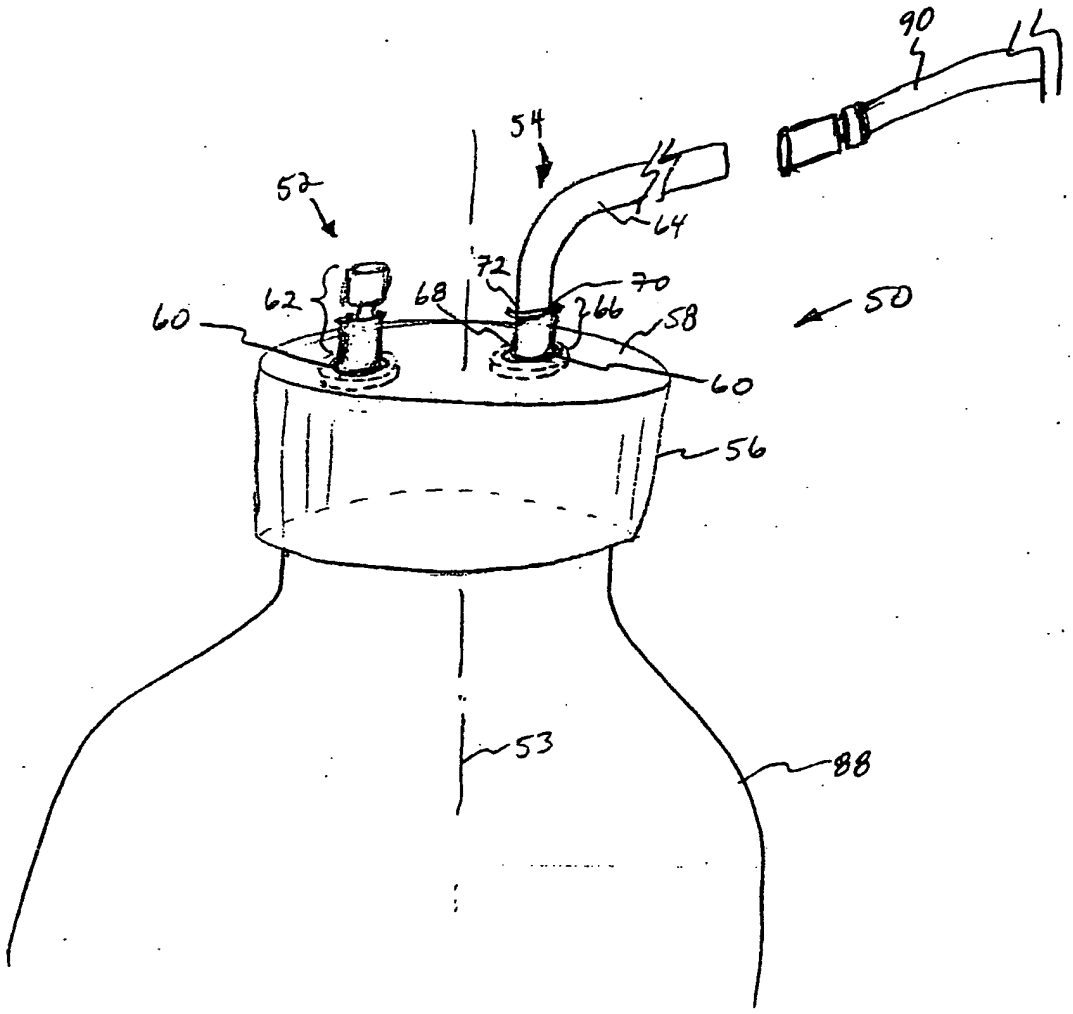

FIGURE 11

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 November 2002 (14.11.2002)

PCT

(10) International Publication Number
WO 02/089725 A3

(51) International Patent Classification[7]: A61M 39/10, A61J 1/00, B01L 3/14

(21) International Application Number: PCT/US02/14849

(22) International Filing Date: 7 May 2002 (07.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/289,429 8 May 2001 (08.05.2001) US

(71) Applicant *(for all designated States except US)*: **NEXELL THERAPEUTICS INC.** [US/US]; 9 Parker, Irvine, CA 92618-1605 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **JULIAR, Rena** [US/US]; 1016 Auburndale Street, Corona, CA 92880 (US). **ETTEFAGH, Guity** [US/US]; 6575 East Paseo Murillo, Anaheim, CA 92807 (US).

(74) Agents: **INSKEEP, James, W.** et al.; Oppenheimer Wolff & Donnelly LLP, 840 Newport Center Drive, Suite 700, Newport Beach, CA 92660-7007 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,

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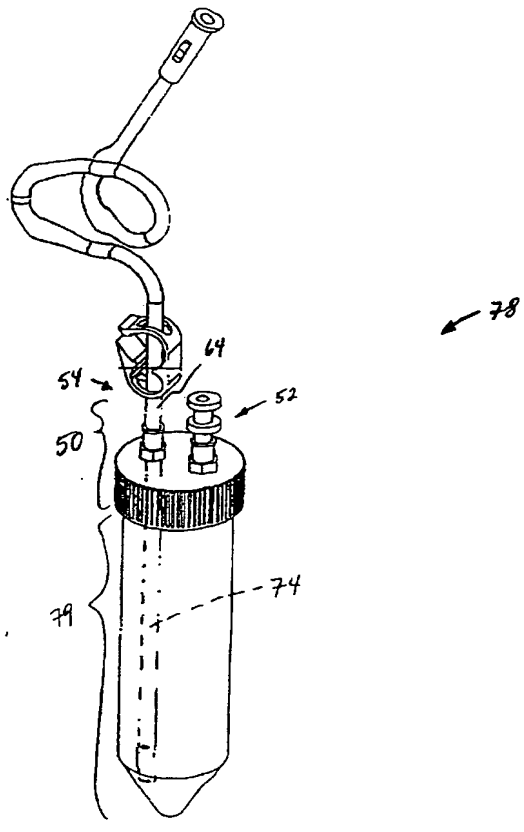
(54) Title: FLUID TRANSFER DEVICES AND METHODS OF USE



(57) Abstract: A device and method of use are disclosed to facilitate fluid transfers during sterile closed system processing procedures. The device is configured to create connections for the transfer of fluid between various components, along a closed sterile fluid passageway and, eventually, either to a fluid container or to a patient. As a result, the device and method of use of the present invention reduce the risk of contamination to the fluids, such as reagents, medicaments and cellular products, and increase user or technician safety during processing procedures.

WO 02/089725 A3

GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
27 November 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/14849

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M39/10 A61J1/00 B01L3/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M A61J B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 034 642 A (ALPHA THERAPEUTIC CORP) 2 September 1981 (1981-09-02) abstract; figure 1 ---	1-10
X	US 4 917 804 A (FRANKS STEPHEN H ET AL) 17 April 1990 (1990-04-17) column 1, line 37 - line 40 column 3, line 19 - line 47 column 4, line 1 - line 18; figure 3 column 5, line 9 - line 12; figure 5 ---	1-8,10
X	US 4 013 076 A (PUDERBAUGH GEORGE ET AL) 22 March 1977 (1977-03-22) column 3, line 20 - line 25 column 3, line 48 - line 68 column 5, line 21 - line 26 figures 1,3 --- -/--	1-3,5-7, 9

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 October 2002	16. 01. 2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lakkis, A

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/14849

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 368 586 A (VAN DER HEIDEN JOHANNES ET AL) 29 November 1994 (1994-11-29) abstract ---	1
A	EP 0 446 713 A (MILES INC) 18 September 1991 (1991-09-18) figure 1 -----	9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/14849

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-10

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-10

   A fluid transfer device comprising a cap-shaped device, a filtration vent and tubing

2. Claims: 11-16

   A method of transferring fluids into or out of a container comprising the steps of: removing a cap from a container while under a laminar flow hood, installing a cap-shaped device onto said container, transferring said container and connecting a closed system set whereby a fluid may be transferred in a closed system fluid pathway

3. Claims: 17-20

   A method of transferring fluids into or out of a container comprising the steps of: adding a fluid via a cap-shaped device, in a closed system fluid pathway, centrifuging said fluid and removing a portion of said fluid while maintaining said closed system fluid pathway

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 02/14849

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 0446713 A2	18-09-1991
		ES 2056508 T3	01-10-1994

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 November 2002 (14.11.2002)

PCT

(10) International Publication Number
WO 2002/089725 A3

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(21) International Application Number: PCT/US2002/014849

(22) International Filing Date: 7 May 2002 (07.05.2002)

(25) Filing Language: English

(26) Publication Language: English

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(71) Applicant *(for all designated States except US)*: **NEXELL THERAPEUTICS INC.** [US/US]; 9 Parker, Irvine, CA 92618-1605 (US).

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(75) Inventors/Applicants *(for US only)*: **JULIAR, Rena** [US/US]; 1016 Auburndale Street, Corona, CA 92880 (US). **ETTEFAGH, Guity** [US/US]; 6575 East Paseo Murillo, Anaheim, CA 92807 (US).

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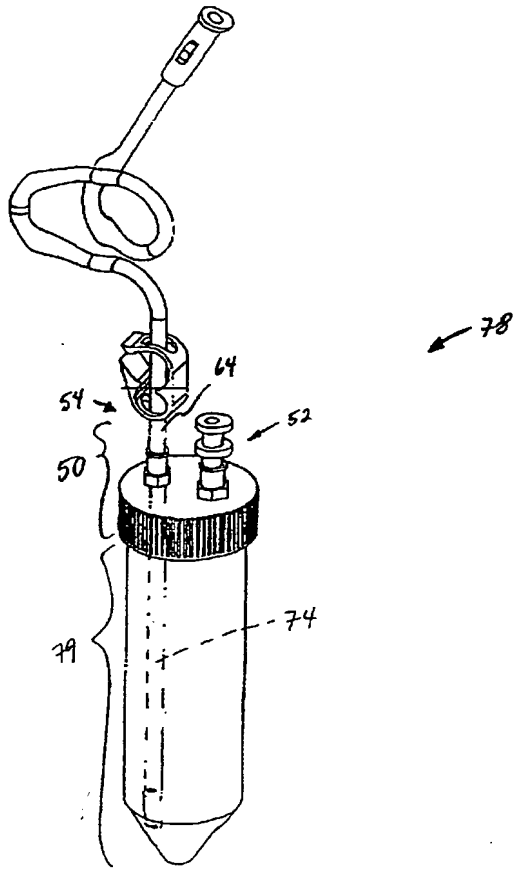
[Continued on next page]

(54) Title: FLUID TRANSFER DEVICES AND METHODS OF USE



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WO 2002/089725 A3

(84) **Designated States** *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

(88) **Date of publication of the international search report:**
27 November 2003

(48) **Date of publication of this corrected version:**
21 May 2004

(15) **Information about Correction:**
see PCT Gazette No. 21/2004 of 21 May 2004, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.